

**Advisory Action
Before the Filing of an Appeal Brief**

Application No. 10/524,817	Applicant(s) MATSUDA ET AL.
Examiner DANA SHIN	Art Unit 1635

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 28 February 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).

5. ☐ Applicant's reply has overcome the following rejection(s): _____.

6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: 1-6.

Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).

9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).

10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.

12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s) _____

13. ☒ Other: See Continuation Sheet

/J. E. Angell/
Primary Examiner, Art Unit 1635

Continuation of 11. does NOT place the application in condition for allowance because: Brown et al. taught that "the phosphodiester linkages of natural RNA are modified to include at least one of a nitrogen or sulfur hetero-atom". See paragraph 0050. Applicant argues that the "4-thio UTP" taught by Brown et al. is a modification incorporated into the "base" not "sugar". Irrespective of the actual location of the "4-thio UTP" modification, Brown et al. clearly taught, suggested, and indeed recommended that the "sugar" of siRNA molecules comprises at least one of sulfur hetero-atom. Furthermore, 4-thio "sugar" compound or moiety was known in the art as early as the year of 1994, as evident by the teachings of Walker et al. (US 5,356,882). See columns 8-10 of the citation. Applicant further argues that the reactions within Burgess et al. do not involve thio-nucleosides and Burgess et al. taught away from the claimed invention because they suggested, "no method for preparing nucleoside triphosphates is suitable for all nucleobase derivatives". It is true that Burgess et al. taught that there is no perfect, single method that can be applied to all nucleobase derivatives and that the efforts to synthesize nucleoside triphosphates have languished during 1990-2000. However, at the same time, Burgess et al. taught that the arena of synthesizing and preparing nucleoside triphosphates "is likely to expand" because of the increasing art-wide demand and need for nucleoside triphosphates, which is triggered by the therapeutic applications of nucleoside triphosphates, and they also encouraged and predicted "a revival of interest in preparations of these important molecules". See page 2058. While acknowledging the fact that there is no single method of preparing nucleoside triphosphates, Burgess et al. taught Yoshikawa's POCI₃ phosphorylation procedure to produce nucleoside monophosphates, and they also suggested direct, one-step triphosphorylation procedures, which could be further developed and modified to facilitate synthesis of nucleoside triphosphates. Hence, this rejection is maintained.

Continuation of 13. Other: No proposed amendments have been filed. PTO-FORM 892 is attached..